Orthogonal Least Squares

Keyphrases □ Linear regression methods—both variables measured subject to error, equations derived □ Orthogonal least squares—linear regression methods, both variables measured subject to error, equations derived

To the Editor:

The usual least-squares linear regression of y on x assumes that y is measured subject to error and that x is fixed or measured without error. The line of best fit:

$$\frac{y-\bar{y}}{s_y} = r\frac{x-\bar{x}}{s_x} \qquad \text{(Eq. 1)}$$

therefore minimizes the sums of squares of vertical deviations (along y) from the set of n observed points $(x_1, y_1), \ldots, (x_n, y_n)$ to this line, where the sample means are $\bar{x} = \Sigma x_i/n$ and $\bar{y} = \Sigma y_i/n$, the sample variances are $s_x^2 = \Sigma(x_i - \bar{x})^2/n$ and $s_y^2 = \Sigma(y_i - \bar{y})/n$, the sample covariance is $s_{xy} = \Sigma(x_i - \bar{x})(y_i - \bar{y})/n$, and the sample correlation coefficient is $r = s_{xy}/s_x s_y$.

The purpose of this communication is to outline the known methods of linear regression when *both* x and y are measured subject to error. Reference is made to statistical textbooks on multivariate analysis.

Morrison (1) considered the problem of the minimization of the sums of squares of *perpendicular* deviations from the points to the line and indicated that it is equivalent to a rotation of axes such that the perpendicular projection of these points onto the new axis has a maximum variance. This approach gives as the line of best fit:

$$\frac{y-\bar{y}}{s_y} = [\text{sign } (r)]\frac{x-\bar{x}}{s_x} \qquad \text{(Eq. 2)}$$

Kendall and Stuart (2) gave a more general model when both x and y are subject to the errors δ and ϵ, respectively. Their development leads to the line of best fit:

$$y - \bar{y} = (x-\bar{x})\frac{(s_y^2 - \lambda s_x^2) + \sqrt{(s_y^2 - \lambda s_x^2)^2 + 4\lambda s_{xy}^2}}{2s_{xy}} \qquad \text{(Eq. 3)}$$

where $\lambda = \sigma_\epsilon^2/\sigma_\delta^2$ is assumed known, σ_ϵ^2 is the population error variance of y, and σ_δ^2 is the population error variance of x.

When $\lambda = 1$, Eq. 3 reduces to Eq. 2; when $\sigma_\delta^2 = 0$, it reduces to Eq. 1. Thus, if both variables are subject to errors of the same magnitude, then Eq. 2 can be used. If the errors differ markedly, Eq. 3 should be used.

(1) D. F. Morrison, "Multivariate Statistical Methods," McGraw-Hill, New York, N.Y., 1967, pp. 84, 85, 230–234.

(2) M. G. Kendall and A. Stuart, "The Advanced Theory of Statistics, vol. 2, Inference and Relationship," 3rd ed., Charles Griffin, London, England, 1973, Sect. 29.9–29.12.

J. R. Howell

Department of Pharmacy and Pharmaceutics
School of Pharmacy
Medical College of Virginia
Virginia Commonwealth University
Richmond, VA 23298

Received March 4, 1976.
Accepted for publication July 27, 1976.

BOOKS

REVIEWS

Progress in Medicinal Chemistry, Vol. 12. Edited by G. P. ELLIS and G. B. WEST. American Elsevier, 52 Vanderbilt Avenue, New York, NY 10017, 1975. 484 pp. 15.5 x 21.5 cm. Price $58.50.

In keeping with the tradition of the series, the editors have assembled excellent reviews of timely topics. The first five of the eight chapters emphasize the utility of specific instrumentation to the study of biological samples.

In Chapter 1, A. M. Lawson and G. H. Draffon briefly describe basic principles of mass spectrometry and GC–mass spectrometry and give attention to developments concerned with the role of computers in data analysis, selected ion monitoring methods, the use of stable isotopes, and alternative ionization processes. Numerous examples of specific applications are presented to demonstrate the present scope of the methods in the areas of biochemistry, pharmacology, and toxicology.

The basic principles, applications, and the more recent technological advances in affinity chromatography, gel chromatography, and high-pressure liquid chromatography are reviewed by K. W. Williams and R. C. Smith in Chapter 2.

P. J. Sadler, in Chapter 3, has chosen examples from recent literature to highlight progress in the NMR study of biological materials. The examples include the use of isotopic labels, paramagnetic probes, and other techniques.

In Chapter 4, D. L. Williams-Smith and S. J. Wyard briefly explain electron spin resonance spectroscopy and review its application to the study of metalloproteins, biological free radicals, and complex multicomponent enzyme systems. Also the use of spin labeling in enzymology, membrane studies, and immunochemistry is discussed.

The application of polarography to analytical and mechanistic problems in biochemistry, pharmacology, and toxicology is reviewed in Chapter 5 by M. Brezina and J. Volke.

The rapidly growing literature on cyclic nucleotides is reviewed by B. G. Benfey in Chapter 6. The discussion includes a review of the methods of determining the cyclic nucleotides as well as assays of certain other enzyme activities.

The increasing importance of *Pseudomonas aeruginosa* as a human pathogen makes Chapter 7 by R. B. Sykes and A. Morris a timely review. The sensitivity of the organism, as well as possible mechanisms by which the organism becomes resistant to various classes of antibacterial agents, is discussed.

The final chapter by J. C. Jaszberenyi and T. E. Gunda is the first of a two-part series (Part II is scheduled to appear in Volume 13 of this series) on the synthetic analogs of the β-lactam antibiotics. This chapter reviews changes in the thiazolidine and thiazine rings as well as substituents on rings. In one section, the literature on the mode of action of these antibotics is discussed from the view of a "structural analog" model *versus* a "conformational response" model.

In the preface, the editors state that "Biochemists, pharmacologists and toxicologists are finding increasing use for methods which have hitherto been used mainly by chemists, and the aim of the first six reviews is to allow biologists to assess the potential value of the techniques in their own work." Therefore, the book should find an interested audience among biochemists, pharmacologists, toxicologists, medicinal, and natural products chemists.

Reviewed by Charles M. Darling
Auburn University
School of Pharmacy
Auburn, AL 36830